

## REMARKS

Claims 14 and 19-25 were pending and rejected. In this Amendment, claims 14 and 19-23 are amended. No new matter is being added.

Claims 14 and 19-23 are amended to improve their readability, and except as otherwise identified below, not to change scope. For example, “one or more computer systems” is amended for readability to read “a computer system,” and the “one or more” remains implicit. (See, e.g., *KCJ Corp. v. Kinetic Concepts, Inc.*, 223 F.3d 1351, 1356 (Fed. Cir. 2000).

Claims 14 and 19-25 are rejected under 35 U.S.C. § 112 first paragraph as including new matter.

Claim 14 as amended reads as follows:

A computer-implemented method of generating a local-global alignment score that indicates a global and a local similarity between a first protein structure and a second protein structure, the method executed by a computer system and comprising:

- receiving, at the computer system, a protein structure correspondence having a plurality of positions indicating a corresponding pair of residues in the first protein structure and the second protein structure;
- determining, by the computer system and according to a plurality of specified threshold values, a plurality of root mean square deviations corresponding to a plurality of sets of pairs of residues, each set including a plurality of pairs of residues that are contiguous in the protein structure correspondences;
- selecting, by the computer system, a longest contiguous segment corresponding to a set of pairs of residues of the plurality of pairs of residues based on the plurality of root mean square deviations;
- determining, by the computer system, a global distance test value based on a plurality of distance scores, each score corresponding to a number of pairs of residues in the correspondence within a pre-defined distance of a plurality of pre-defined distances;
- generating, by the computer system, the local-global alignment score based on the longest contiguous segment and the global distance test value; and
- providing, by the computer system, a result based on the local-global alignment score.

The Examiner argued that the previously claimed steps of identifying distance scores and selecting a global distance test value were not supported. Applicant disagrees with the Examiner, but in light of the amendment to claim 14, the point is now moot. The claim is amended to recite that a global distance test value is determined based on a plurality of distance scores corresponding to residues in the

correspondence within a pre-defined distance of a plurality of pre-defined distances. As the Examiner previously noted, the specification discloses how to determine a GDT value. Because the claimed step is supported by the specification, the rejection should be withdrawn. In addition, the claim is amended to clarify that the step of determining RMSD is performed according to specified threshold values. This addresses the Examiner's concern regarding the support for that limitation, and thus the rejection of that limitation should now be withdrawn as well.

The Examiner also maintained the rejection of claims 14 and 19-25 under 35 U.S.C. § 103(a) as unpatentable over Zemla et al. and Cristobal et al.

Applicant previously provided a declaration by Dr. Zemla, and which the Examiner discussed in the most recent office action. Dr. Zemla discusses his article, "LGA, a method for finding 3D similarities in protein structures", *Nucleic Acids Research*, 2003, Vol. 31 ("Zemla NAR"), e.g., at paragraphs 11-14 of his declaration. Dr. Zemla notes in footnote 1 that the text of that article is "largely incorporated by reference into the priority document of the instant application". The Examiner disputes this statement, but in the provisional application (60/451,292) includes a paper by the same name beginning at the page marked "4". As Dr. Zemla noted, the text of Zemla NAR and the paper forming part of the provisional largely overlap, and the portions of Zemla NAR quoted in the declaration appear almost verbatim in the provisional application as well. For example, the initial quotation found in paragraph 11 of Dr. Zemla's declaration appears at page 1, col. 2, lines 12-20 of Zemla NAR, and a substantively similar portion can be found in the final two paragraphs of page 4 of the provisional application.

Dr. Zemla also provided evidence for his belief that generating a single local-global alignment score, based on a longest contiguous segment selected based on a plurality of root mean square deviations determined using a plurality of specified threshold values and global distance test values selected based on a plurality of distance scores that represent a number of pairs of residues within a pre-defined distance of a plurality of pre-defined distances produces unexpected results as compared to the methods described in the art cited by the Examiner.

As Dr. Zemla notes, in previous protein structure homology algorithms, including those cited, an alignment is generated using a set of internal parameters, and the alignment is then scored. An optimization function uses a function to evaluate the

goodness of the alignment, e.g., a RMSD. In the claimed invention, the LCS and GDT value are selected based on a plurality of RMSD values and a plurality of distance values, respectively. These values are generated based on a plurality of different parameters (threshold values and predefined distances). This allows intermediate local and global alignments to be evaluated and selected.

Dr. Zemla notes that for a set of aligned structures, the optimal threshold value and predefined distances cannot be determined a priori. Thus, using a single threshold value and pre-defined distance leads to a sub-optimal alignment. In contrast, the claimed invention evaluates the intermediate local and global alignments to select the best local and global alignments.

Thus, neither of the cited references renders obvious for purposes of § 103 the claimed invention, including the steps of “determining, by the computer system, a global distance test value based on a plurality of distance scores, each score corresponding to a number of pairs of residues in the correspondence within a pre-defined distance of a plurality of pre-defined distances,” or “generating, by the computer system, the local-global alignment score based on the longest contiguous segment and the global distance test value,” or of “providing, by the computer system, a result based on the local-global alignment score.”

Accordingly claim 14 is patentable over the cited references. Dependent claims 19-25 are also patentable over the cited references as each depends from a patentable independent claim in addition to reciting its own patentable features.

The Examiner is asked to contact the undersigned attorney to advance prosecution, and prior to issuing a subsequent office action.

Respectfully submitted,

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